REMARKS

Claims 1-42 are pending. Claims 11, 17-35 were withdrawn. Claims 1-10, 12-16 and 36-42 were examined and rejected.

The claims are not amended.

In view of the following remarks, reconsideration of this application is respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 1-10 and 12-16 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lappin (J. Mol. Diagnostics, 2001 3:178-188). The Applicants respectfully traverse this rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Additionally, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1566 (Fed. Cir. 1990).

The rejected claims are directed to a method of producing a biopolymeric array. The method includes immobilizing a population of a number of copies of a probe for a target to a surface of a solid support. Elements of the claimed method include:

determining an anticipated abundance of a target in a sample for which said array is designed to assay;

identifying a number of copies of a first probe for said first target, wherein said identified number of copies is dependent on said determined anticipated abundance; and

immobilizing a first population of said number of copies of a first probe for said first target to a surface of a solid support to produce said biopolymeric array.

The Applicants submit that Lappin discloses neither “determining an anticipated abundance of a target in a sample”, nor “identifying a number of copies of a first probe for said first target, wherein said identified number of copies is dependent on said determined anticipated abundance” as required by the instant

claims. As such, Lappin cannot anticipate the rejected claims, and this rejection should be withdrawn.

In attempting to establish this rejection, the Examiner argues that Lappin discloses the claimed method because Lappin's method includes optimizing the concentration of oligonucleotide probes, and then fabricating an array containing probes at optimized concentration. However, at no point does Lappin determine an anticipated abundance of a target in a sample, as required by the claims.

The Applicants acknowledge that Lappin performs a titration experiment in which probes of different concentration are hybridized with a labeled target. The results of this experiment are shown in Fig. 5. However, the Applicants believe that this titration experiment does not result in a determination of an anticipated abundance of the target to which that probe binds. Rather, Lappin's probe titration experiment optimizes probe concentration for physical variation in the probes themselves (e.g., the differences in T_ms, sequence, G/C richness, degree of secondary structure, batch, etc., between the different probes). Since Lappin's probes are quite small (many of probes are 20-mers; see Table 1B), and Lappin's hybridization temperatures are quite low (see, p. 179, col. 2,), such physical variation would be expected to yield a very wide range of signal intensities when hybridized with a labeled target.

As such, Lappin's probe titration experiment cannot be used to determine the abundances of the targets to which the probes bind. Rather Lappin's probe titration experiment teaches how to increase signal to noise ratio for detecting a particular target using a particular probe. Lappin's method is used for determining the best concentration of probe to be used when the probe sequence cannot be changed as it is designed to pick up certain mutations. Lappin's method is designed to pick out the best probe concentration to detect a target.

Moreover, the samples under analysis in Lappin's disclosure are *genomic* samples. Since the relative number of sequences in a genomic sample would be expected to be similar, if not identical, there would be no need for Lappin to determine an anticipated abundance of a target in the sample, identify a number of copies of a first probe for a target, and then immobilize a first population of the number of copies on an array, as required by the rejected claims. The relative

abundance of the target is not an issue because the target is a genomic sample and all genes are present in the same number of copies in a genomic sample.

In view of the foregoing discussion that Lappin discloses neither "determines an anticipated abundance of a target in a sample", nor "identifying a number of copies of a first probe for said first target, wherein said identified number of copies is dependent on said determined anticipated abundance" as required by the instant claims. As such, Lappin cannot anticipate the claims, and this rejection should be withdrawn.

Furthermore, claim 2 depends from claim 1 and further recites the requirement for a probe density that is in the range of 0.001 pmoles/mm^2 to about 10 pmoles/mm^2. Such a range is not disclosed in Lappin. The Examiner has not addressed claim 2 under the § 102 rejection. As such the rejection of claim 2 under § 102 should be withdrawn.

Claim 3 is indirectly dependent on claim 1 and further requires that the first population of the number of copies determined by the method of claim 1 is present in at least two replicate features. Replicate features are not disclosed in Lappin. The Examiner has not addressed claim 3 under the § 102 rejection. As such the rejection of claim 3 under § 102 should be withdrawn.

Claims 4 and 5 recite particular probe densities and number of probe copies, respectively. Probe densities and number of probe copies are not disclosed in Lappin. The Examiner has not addressed claims 4 and 5 under the § 102 rejection. As such the rejection of claims 4 and 5 under § 102 should be withdrawn.

Claim 14 indirectly depends from claim 1, and further requires that the probes be at a density that is dependent on the anticipated abundance of the target. The section of Lappin pointed to by the Examiner does not mention probe density. Since the element of probe density is missing from the cited reference, it cannot be used to anticipate the claim.

For these additional reasons, Lappin fails to anticipate the instant claims under § 102. As such this rejection may be withdrawn. Withdrawal of this rejection is requested.

Claim Rejections – 35 U.S.C. § 103

Claims 2-5 and 36-42 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Lappin in view of Rothberg (U.S. 6,355,423). As best understood by the Applicants, the Examiner believes that Lappin's method of making a probe-optimized array, in combination with Rothberg's array densities, renders the claims obvious. The Applicants respectfully traverse this rejection.

The Patent Office has recently published guidelines for determining obviousness under 35 U.S.C. §103 in view of the KSR decision. These guidelines, termed the "Obviousness Guidelines" are found in the Federal Register Vol. 72, No. 195 (published Wednesday, October 10, 2007) and should be followed by Examiner in evaluating whether a claim is obvious.

According to the Obviousness Guidelines, when Office personnel reject claims by attempting to combine prior art elements according to allegedly known methods to yield predictable results, the Office must resolve the Graham factual inquiries and articulate:

(1) "a finding that **the prior art included each element claimed**, although not necessarily in a single prior art reference, with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art reference;"

(2) "a finding that one of ordinary skill in the art could have combined the elements as claimed by known methods, and that in combination, each element merely would have performed the same function as it did separately; and"

(3) "a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable." (Federal Register / Vol. 72, No. 195 / Wednesday, October 10, 2007 / Notices at 57529, *citing KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (US 2007).

Thus, the rationale to support a conclusion that a claim would have been obvious is that "**all the claimed elements were known in the prior art** and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions," and that "the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention." *Id.* at 57529.

As noted above, Lappin is deficient in that it fails to teach or disclose any step that requires determining an anticipated abundance of a target in a sample, as required by the instant claims.

Rothberg, relied upon solely to provide array densities, also fails to disclose any step that requires determining an anticipated abundance of a target in a sample. As such Rothberg cannot meet Lappin's deficiency.

As such, the cited references, taken alone or in any combination, fail to teach or suggest all of the elements of the rejected claims. As such, under current law, the cited references cannot render the rejected claims obvious.

Furthermore, Claim 3 which is indirectly dependent on claim 1 further requires that the first population of the number of copies determined by the method of claim 1 be present in at least two replicate features. To reject this claim as obvious, the Examiner has stated that on p. 186 Lappin discloses 7 replicate features. However, these replicate features are not the same as being taught by claim 3. The replicate features of claim 3 have the same number of copies, this number being determined by the method of claim 1. The 7 replicate features pointed to by the Examiner are in fact not replicates as they are of different concentrations (1, 3.3, 5, 10, 20, 50 and 100μM).

Claim 4 depends from claim 3 and further requires that each of said replicate features comprises probes at a density that ranges from 0.001 pmoles/mm^2 to about 10 pmoles/mm^2. Lappin does not disclose at least two *replicate features* comprising first population of number of copies of a first probe determined by the method of claim 1. Since Rothberg is cited solely for its teachings of array density, Lappin in view of Rothberg cannot render this claim obvious.

For these additional reasons, claims 2-5 and 36-42 are not obvious under § 103. The Applicants submit that this rejection has been adequately addressed and may be withdrawn. Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone James Keddie at (650) 833-7713.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10031014-1.

Respectfully submitted,

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